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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/613,739	07/03/2003	Arthur M. Krieg	C01037.70043.US	4713

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EXAMINER	
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ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/613,739	KRIEG, ARTHUR M.	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03/26/07*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,16-20,22,27,28,30,31 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 June 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/08/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-20, 22, 27-32, 43, 45-57, 63-65, 70-73, 76-80, 83-84, 88-89, 94-95 and 97-98, as presented by Applicant.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 10-15, 29, 32, 45-57, 63-65, 70-73, 76-80, 83-84, 88-89, 94-95, and 97-98 , as presented by Applicant.

DETAILED ACTION

Status of Claims

1. Claims 21, 23-26, 33-42, 44, 58-62, 66-69, 74-75, 81-82, 85-87, 90-93 and 96 are cancelled, per Applicant's 10/31/2003 submission. Claims 1-20, 22, 27-32, 43, 45-57, 63-65, 70-73, 76-80, 83-84, 88-89, 94-95 and 97-98 are pending. Claims 10-15, 29, 32, 45-57, 63-65, 70-73, 76-80, 83-84, 88-89, 94-95, and 97-98 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 03/09/2006. Claims 1-9, 16-20, 22, 27-28, 30-31 and 43 are under examination.

It is noted that Applicant submits that claims "1-21, 23, 28-33, 44, 46-58, 64-66, 71-74, 77-81, 84-85, 89-90, 95-96 and 98-99 are pending." However, it is found that this is not the case. Claims 1-20, 22, 27-32, 43, 45-57, 63-65, 70-73, 76-80, 83-84, 88-89, 94-95 and 97-98 are pending.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-9, 16-20, 22, 27-28, 30-31 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krieg et al.[1]

In response to the rejection, Applicant submits that that one of ordinary skill in the art would not be motivated to modify the sequence disclosed as SEQ ID NO: 888 to produce the sequence of SEQ ID NO: 1, by changing the nucleic acid residue at position 20 of SEQ ID NO: 888 from A to T because Krieg et al. does not suggest such changes. Specifically, Applicant submits that there is no motivation for one of ordinary skill in the art to make a single nucleic acid substitution to one nucleic acid molecule based on the results of a structurally different nucleic acid sequence, directing to the structural difference between SEQ ID NO: 888 and SEQ ID NO: 320.

Applicant's submission has been considered, however, it is not found persuasive. In the instant case, Krieg et al. teaches SEQ ID NO: 888, which has the sequence TCGTCGTTTCGTCGTTTTGACGTT. SEQ ID NO: 888 of Krieg et al. comprises the GACGTT motif and is a T rich oligonucleotide. In determining the optimal CpG motif for stimulation of an immune response in humans and non-rodent vertebrates for use in combination with a T rich oligonucleotide, Krieg et al. took the GACGTT motif via SEQ ID NO: 320 and modified the nucleic acids, by substituting/replacing or exchanging the existing nucleic acid(s) with another nucleic acid, flanking the CpG motif. [Example 9, Line 24, page 142 to line 20, page 143, in particular.] In a methodical substitution of nucleic acids process, Krieg et al. exchanged adenine (the A in the GACGTT motif) with thymine. This exchange renders the GACGTT motif to GTCGTT motif. Krieg et al.

[1] Krieg et al. WO 2001/22972, published April 05, 2001.

teaches that this modified motif, GTCGTT has a slightly higher activity. In view of this, it would have been prima facie obvious for one of ordinary skill in the art to follow the teachings of Krieg et al. and modify the GACGTT motif present in SEQ ID NO: 888 of Krieg et al. to TCGTT. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to optimize the immune response induced by the T rich oligonucleotide of SEQ ID NO: 888. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the determination of a workable range or optimal range is routinely practiced in the art.

It is further noted that Applicant submits that one of ordinary skill in the art would have no expectation of success that making a change that resulted in slightly higher activity in SEQ ID NO: 320.

Applicant's submission has been considered, however, it is not found persuasive. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for enhancing the immunostimulatory activity of the immunostimulatory nucleic acid because Krieg et al. clearly teaches that the GTCGTT motif, which Krieg et al. teaches as a human immunostimulatory motif, is more immunostimulatory than the GACGTT motif, mouse immunostimulatory motif. [Lines 10-12, page 154, in particular.] Additionally, Applicant has not provided any evidence showing otherwise. Additionally, even if enhancement of immunostimulatory activity is not accomplished, it remains that Krieg et al. suggests the use of the human motif over the mouse motif. Thus, as mentioned above, one of ordinary skill in the art, at the time

the invention was made, would have been motivated to do so to optimize the immune response induced by the T rich oligonucleotide of SEQ ID NO: 888. As previously presented, the claims are directed toward a composition comprising an immunostimulatory nucleic acid comprising the nucleic acid sequence of SEQ ID NO:1. Claim 3, which depends on independent claim 1, requires the composition to further comprise an antigen, which is later limited to a microbial antigen by claim 4. Claim 5 further limits the microbial antigen of claim 4 to a viral antigen. Claim 6 additionally limits the antigen of claim 3 to those encoded by a nucleic acid vector. Claim 7, which is interpreted to recite a dependency to claim 6, requires that the nucleic acid vector be different from the immunostimulatory nucleic acid. Claim 8 further limits the antigen of claim 3 to a peptide antigen. Claim 9, which depends on claim 1, requires the composition to further comprise an adjuvant. Claim 16 (currently incorrectly listed as claim 17) requires the immunostimulatory nucleic acid to have a nucleic acid backbone that is modified. Claim 17 (currently incorrectly listed as claim 18), which depends on claim 16, requires the modification to be a phosphorothioate modification. Claim 18 currently incorrectly listed as claim 19), which depends on claim 16, requires the modified backbone to a chimeric backbone. Claim 19 (currently incorrectly listed as claim 20), which depends on claim 16, requires the immunostimulatory nucleic acid to have all modified backbones. Claim 20, (currently incorrectly listed as claim 21), which depends on claim 1, requires the composition to comprise a pharmaceutically acceptable carrier. Claim 22 (currently incorrectly listed as claim 23), which depends on claim 1, requires the immunostimulatory nucleic acid to comprise at least four CpG

motifs. Claim 27 (currently incorrectly listed as claim 28), which depends on claim 1, requires the immunostimulatory nucleic acid to be formulated as a nutritional supplement. Claim 28 (currently incorrectly listed as claim 29), which depends on claim 28, requires the supplement be formulated as a capsule, pill, or a sublingual tablet. Claim 30 (currently incorrectly listed as claim 31), which depends on claim 1, requires the immunostimulatory nucleic acid be formulated for parenteral administration. Claim 31 (currently incorrectly listed as claim 32), which depends on claim 1, requires the immunostimulatory nucleic acid be formulated in a sustained released device. Claim 43 (currently incorrectly listed as claim 44), further limits the sustained release to a microparticle.

Additionally, claim 2, which depends on claim 1, limits the immunostimulatory nucleic acid sequence to consist of SEQ ID NO: 1. SEQ ID NO: 1 has the following sequence: TCGTCGTTTCGTCGTTTTGTCGTT.

Krieg et al. teaches a composition comprising of an immunostimulatory nucleic acid, wherein the immunostimulatory nucleic acid sequence consists of the sequence: TCGTCGTTTCGTCGTTTTGACGTT, SEQ ID NO: 888. SEQ ID NO: 888 of Krieg et al. has at least 4 CpG motifs and is 24 nucleic acid resides in length. The number of CpG motifs and nucleic acid residues present in SEQ ID NO: 888 of Krieg et al. is the same as that of Applicant's claimed SEQ ID NO: 1. The difference between SEQ ID NO: 888 of Krieg et al. and Applicant's claimed SEQ ID NO: 1 is: Nucleic acid residue at position 20 of the sequences are not the same. Nucleic acid residue at position 20 of SEQ ID NO: 888 of Krieg et al. is A (adenine), and the nucleic acid residue at position 20 of

Applicant's claimed SEQ ID NO: 1 is T (thymidine). However, Krieg et al. suggests the exchange of the adenine with thymidine. [Lines 19-20, page 143, in particular.] Krieg et al. notes that the exchange resulted in slightly higher immunostimulatory activity induced by the immunostimulatory nucleic acid. Thus, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to have exchanged adenine for thymidine. One of ordinary skill in the art at the time the invention was made would have been motivated to do so enhance the immunostimulatory activity of the immunostimulatory nucleic acid. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because Krieg et al have demonstrated the enhancement of immunostimulatory activity.

Krieg et al. further teaches the addition of an antigen to the composition. [Lines 19-21, page 6; Lines 3-5, page 38, in particular.] The antigen that Krieg et al. teaches includes microbial antigens, viral antigens, antigens encoded by a nucleic acid vector, and a peptide antigen. [Claims 38-39, page 160, in particular.] The nucleic acid vector that Krieg et al. teaches is different from the immunostimulatory nucleic acid. Krieg et al. also teaches the use of adjuvants with the composition. [Lines 15-16, page 94, in particular.] Krieg et al. additionally teaches the use of nucleic acid backbones that are modified. [Claim 18, page 158, in particular.] The modified backbone that Krieg et al. teaches includes phosphorothioate backbones and chimeric backbones. [Claims 19-20, page 158, in particular] Krieg et al. also teaches modifying all the backbones. [Claim 21, page 158, in particular.]

Krieg et al. also teaches the addition of a pharmaceutically acceptable carrier with the composition. [Lines 1-3, page 3, in particular.] Krieg et al. further teaches that the composition be formulated as a nutritional supplement. [Lines 25-28, page 6, in particular] Krieg et al. teaches that the supplement be formulated as a capsule, pill, or a sublingual tablet. Krieg et al. further teaches providing the composition in a form ready for parenteral administration. [Lines 10-15, page 13, in particular.] Krieg et al. additionally teaches the sustained release, specifically microparticle, form of the composition. [Lines 12-13, page 10, in particular.]

Conclusion

4. No claims are allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bruce R. Campell/
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